

## **Handout for AAAAI Workshop 1212:**

### **Patch testing**

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#### **Selection of Foods:**

- Careful diet history is obtained. For eosinophilic esophagitis, skin testing and patch testing are performed to foods that are in child's diet.
- Current general screen is: Milk, Egg, Soy, Peanut, Wheat, Rice, Corn, Oat, Barley, Potato, Beef, Chicken, Ham, Lamb, Turkey, Pea, Green Bean, Carrot, Peach, Apple – although other foods can be performed.
- A negative control is included with patch testing (either saline or blank chamber)
- Patients must be off oral steroids or other systemic immunosuppressants for one month before testing – topical immunosuppressants (protopic, elidel, and topical steroids should not be used at the site for one week prior to application.

#### **Supplies:**

- Dry powder foods: milk, egg, soy, wheat, rice, corn, oat, barley, potato: purchased in one pound bags from: [www.Barryfarm.com](http://www.Barryfarm.com), peanut from [www.ByrdMill.com](http://www.ByrdMill.com), or other reliable sources
- Jarred single ingredient baby foods (pureed): purchased over the counter at grocery stores, Beechnut has no "added" ingredients: beef, chicken, ham, lamb, turkey, peas, green beans, carrot, peach, apple
- Patches: Finn Chambers, patch trays, patch covers, are available from [www.allerderm.com](http://www.allerderm.com), Finn chambers are available in two sizes: 8mm and 12mm, the selection of foods and size chamber is per the attending physician.
- Gram scale for weight powders
- Sharpie type pen, gauze, applicator, medical tape

#### **Preparation:**

- Weigh out appropriate amounts of foods
  - Dry powders: 1 gram powder in 1 ml sterile water for egg, soy, peanut, wheat, corn, rice, oat, barley, potato; 3 grams powder in 1ml for milk—want nice "pasty consistency"

- Pureed or baby foods (meats, vegetables, fruits): 1 tablespoon onto filter paper to absorb excess fluid
- Load all prepared foods (except rice and corn-only liquid expels when placed in a syringe) into 3 ml oral syringe, label syringes
- Place Finn chambers (strip of 10, strip of 5, or single large 12mm chamber) on patch tray, mark patch strip with the ordered foods (this allows for correct placement and positioning of patches, and for mapping the patches once placed)
- Place foods into the aluminum discs –enough food to cover the bottom of the disc, either by injecting from syringe, or using a stiff applicator (coffee stirrer, cotton tipped applicator=Q-tip on a long wooden stick)
- Milk is always in large Finn chamber
- Cover the tray and bring into room of patient

### **Application:**

- Have parent or older child remove or lift up clothing to expose back. Locate area on back where there is ample and relatively flat space to apply patches. Clean off selected area on back with alcohol prep pad and let dry.
- Gently remove the paper from the unexposed covered edge of patch, and place patches on desired location, holding the patch taut immediately prior to application to avoid wrinkling, bulging, buckling of the patch sticker, apply from bottom up
- Once the patches have been put in place, seal the patch sticker around each well by gently rubbing a finger over the tape surrounding the individual wells, making certain that the wells are sealed by the tape. Tap each well to assure skin contact (48 hours of direct skin contact for results)
- After all wells have been sealed, take a black Sharpie marker, and place a dot on the skin next to the individual wells.
- If the patches appear not to be sticking well, medical tape can be applied to help secure the patches to the skin. If taping, make certain that the patches are flat, with all wells in direct contact with the skin.
- Draw a basic map on the patch testing written record (or other appropriate place in chart) indicating where on the back the patches are, and order of foods on patches.

### **Positioning:**

- Avoid applying patches on areas such as the scapular edges and places that may undergo a good bit of motion.
- For older children, have them stand straight with their shoulders back

- For infants, have the parents hold the child with their faces toward the parent.
- For younger children, have them sit in their parents laps, facing the parent and sit as straight as possible.

**Teaching Items for parents:**

- Keep child's back dry until time of patch removal-48 hours minimum from time of application
- Tell parents the importance of the wells being in direct contact with the skin for 48 hours. If the parent notices that a patch is beginning to come off, re-tape.
- If areas are pruritic, may treat with antihistamine.
- After 48 hours, parents will gently remove patches-they will need to get them wet: bath or shower, with lots of warm soapy water, or slather baby oil over patches and skin to help them "slip" off
- Encourage parents to leave some of the sharpie marker on the skin, to aide in reading the patch tests.
- Provide family with day and after hours telephone numbers in case of questions/concerns.
- Remind families of follow up appointment 72 hours after patch application.

**Documentation:**

- Document in progress note number of patches placed.
- Retain order sheet with placement diagram for patch reading in 72 hours



# Demystifying eosinophilic esophagitis

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# Disclosures

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- No interest in any pharmaceutical company
- Clinical Research project with:
  - Ception
  - Meritage



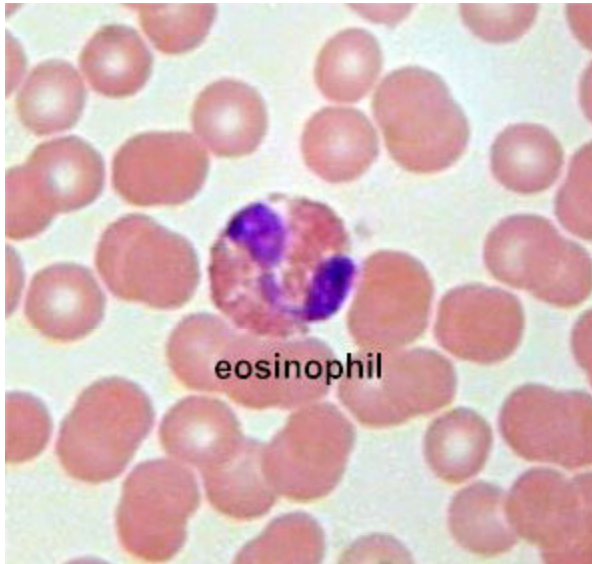
# Goals of the talk

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- Review definitions
- Review CHOP's experience in terms of numbers of patients seen, presentation, and associated conditions
- Review evaluation and treatment options in patients with eosinophilic esophagitis
- Review a few case reports.



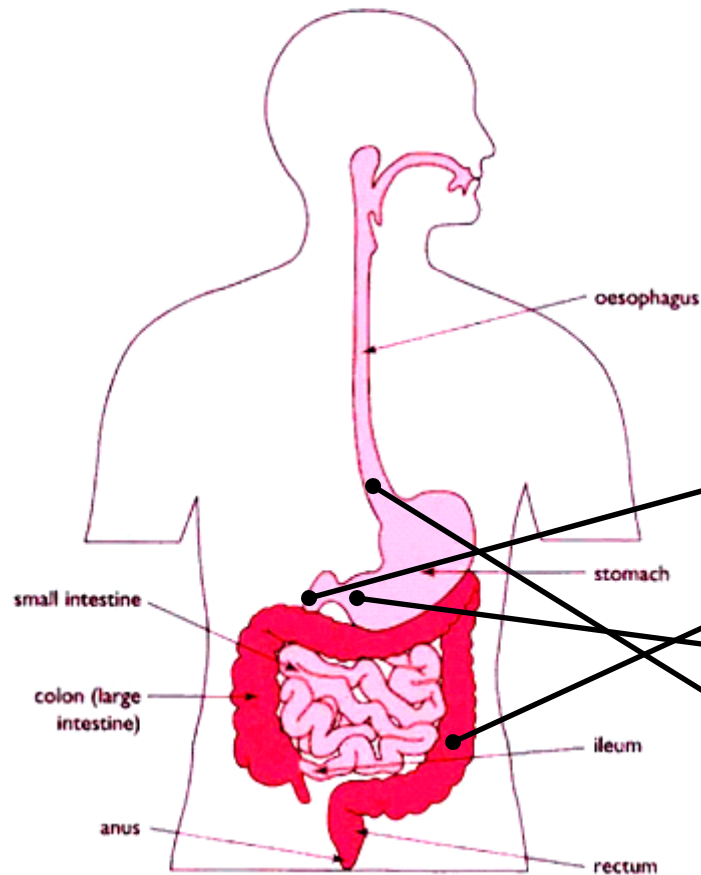
# The Eosinophil



- Accumulates in tissues
- Recruited by:
  - Eotaxin
  - Cytokines (IL5, IL13)
  - Granulocyte-macrophage stimulating factor
- Release toxic granular proteins to cause tissue damage
- In EE, other cells also play role

# Gastrointestinal eosinophils

Normal values, per 400x  
microscopic field:



- Duodenum (20)
- Colon (10-20)
- Gastric antrum (10)
- Esophagus (0)

•> 98% reported EG cases involve antrum and/or duodenum





## Definition of eosinophilic esophagitis

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- Persistent symptoms on a PPI (compliant)
- Endoscopy is performed 8 weeks after initiation of PPI, and biopsy reveals  $\geq 15$  eos/hpf in esophagus
- Approximately 5 to 10% of pediatric patients and 6% of adult patients with poorly controlled GERD are thought to have EE
- Chronic condition



# Clinical presentation

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- Clinical presentation varies per age
  - GERD symptoms (more in infants/younger children)
    - Vomiting, regurgitation, FTT
    - Heartburn, epigastric pain
  - Abdominal pain in school age kids
  - Dysphagia (more in adolescents and adults)
    - Often symptoms intermittent
  - Male > Female



# Eosinophilic esophagitis

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## ■ Eosinophilic Esophagitis

- Intermittent symptoms\*
- pH probe
  - Normal
- Acid blockade
  - Unresponsive
- $\geq 15$  eos/HPF

■ \*can be persistent

## ■ Gastroesophageal Reflux

- Persistent symptoms
- pH probe
  - Abnormal
- Acid blockade
  - Responsive
- 1-5 eos/HPF

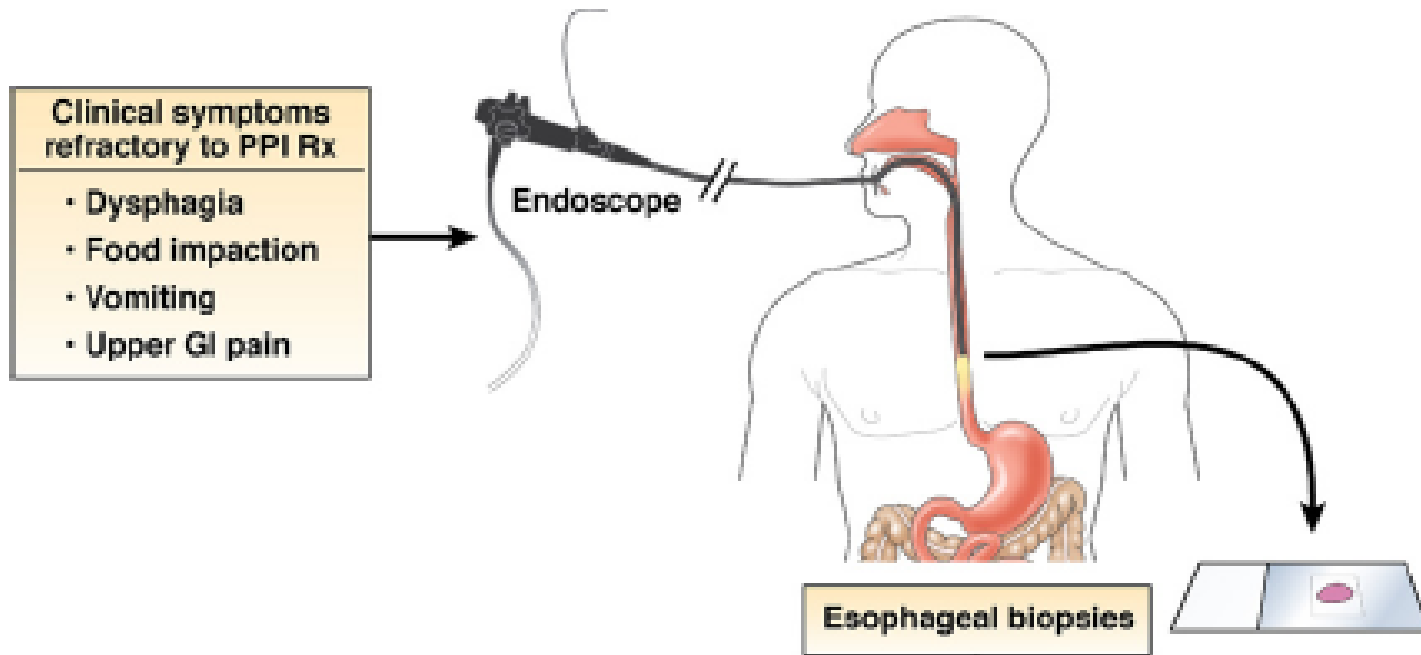


## Presentations: EE vs non-EE

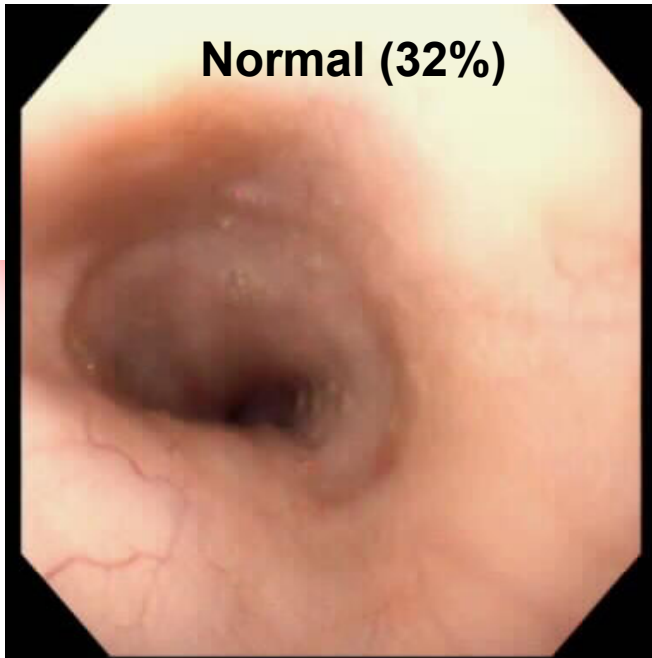
<b>Clinical characteristics</b>	<b>EE</b>	<b>Non-EE</b>
Male	75%	60%
Dysphagia	37%	16%
Abdominal pain	68%	61%
Vomiting	50%	50%
Fundoplication	10%	2%

Thus, biopsy is necessary if persistent symptoms!

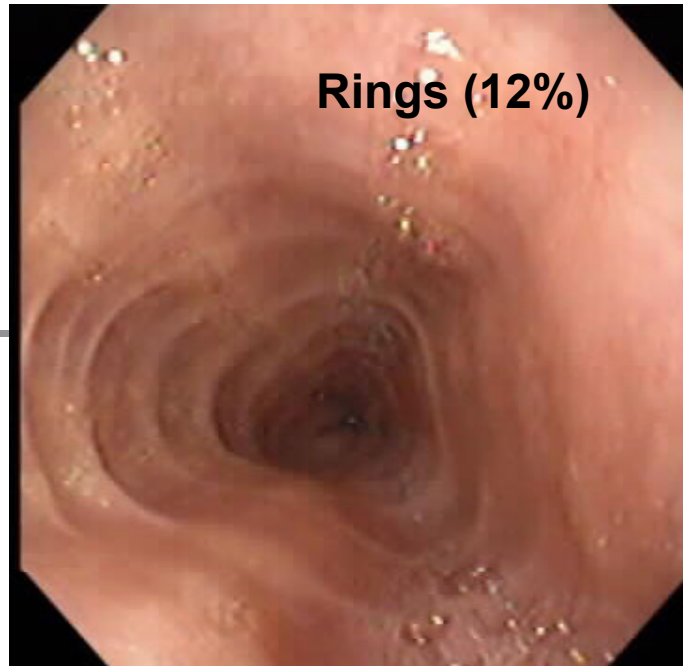
# Eosinophilic esophagitis



**Normal (32%)**



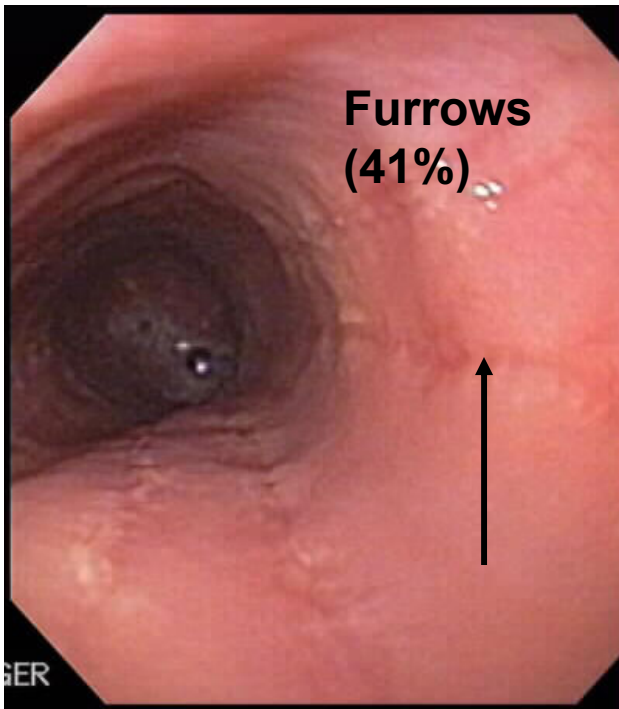
**Rings (12%)**



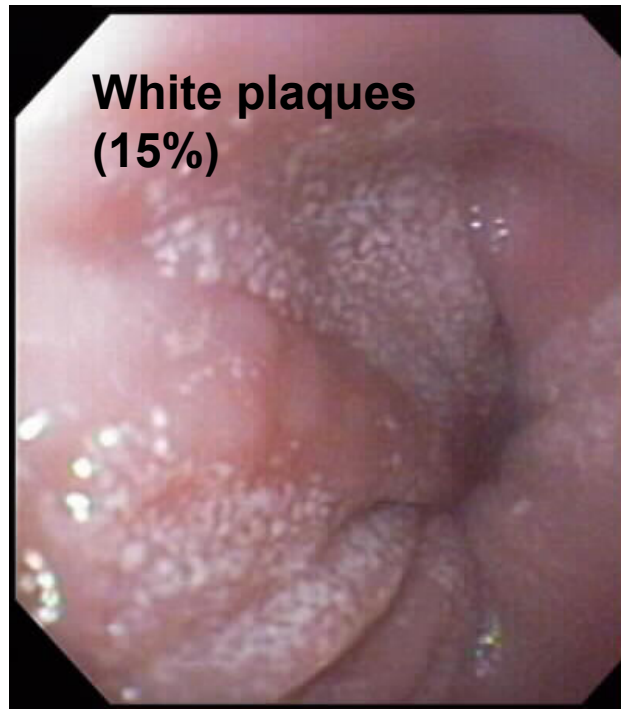
**Diagnosis:**

Biopsy is  
key!

**Furrows  
(41%)**



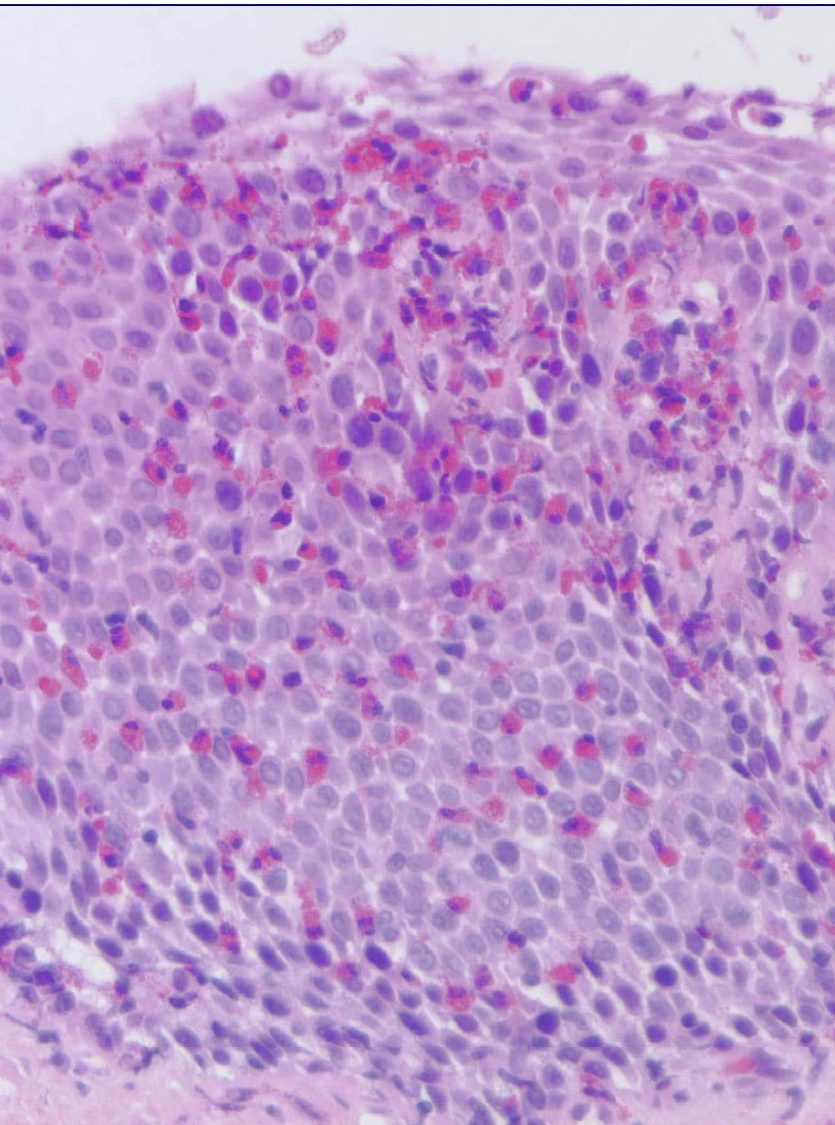
**White plaques  
(15%)**



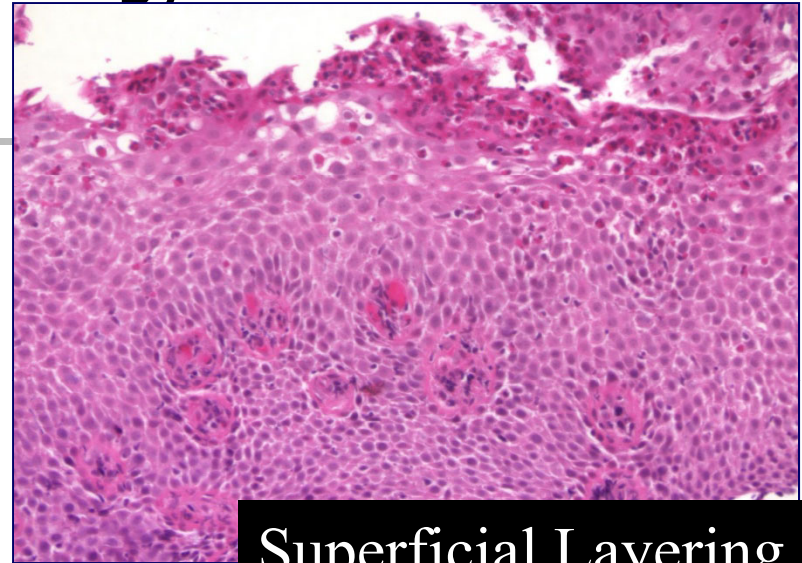


# Eosinophilic Esophagitis

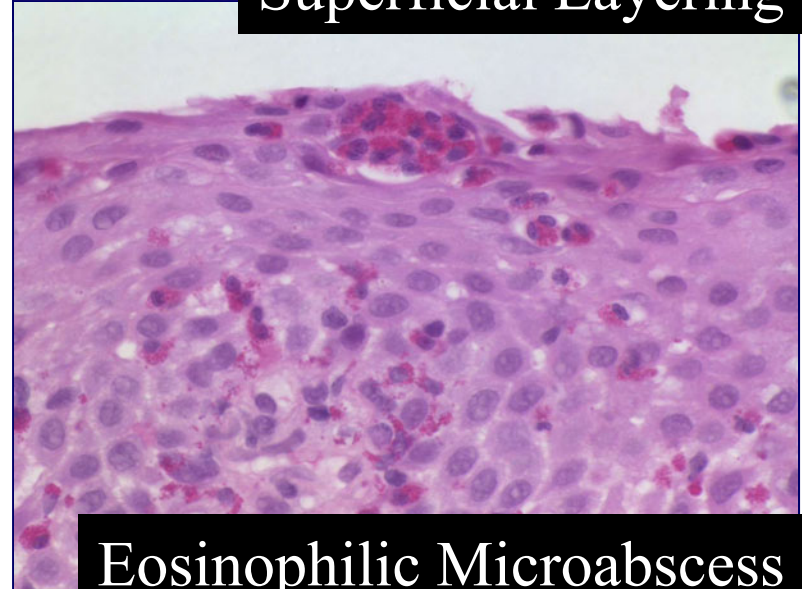
## Histology



**Severe Eosinophilia**



**Superficial Layering**



**Eosinophilic Microabscess**



# Differential diagnosis

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- Eosinophilic gastroenteritis
- Crohn's disease; inflammatory bowel disease
- Medication
- Infection
  - Viral
  - Candidal
  - Parasitic
- Hypereosinophilic syndrome

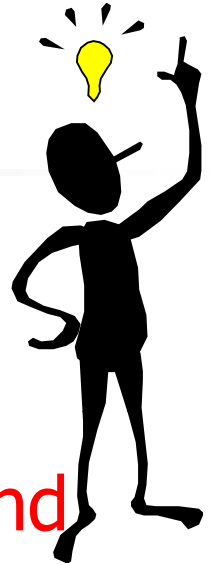




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# What are CHOP statistics?

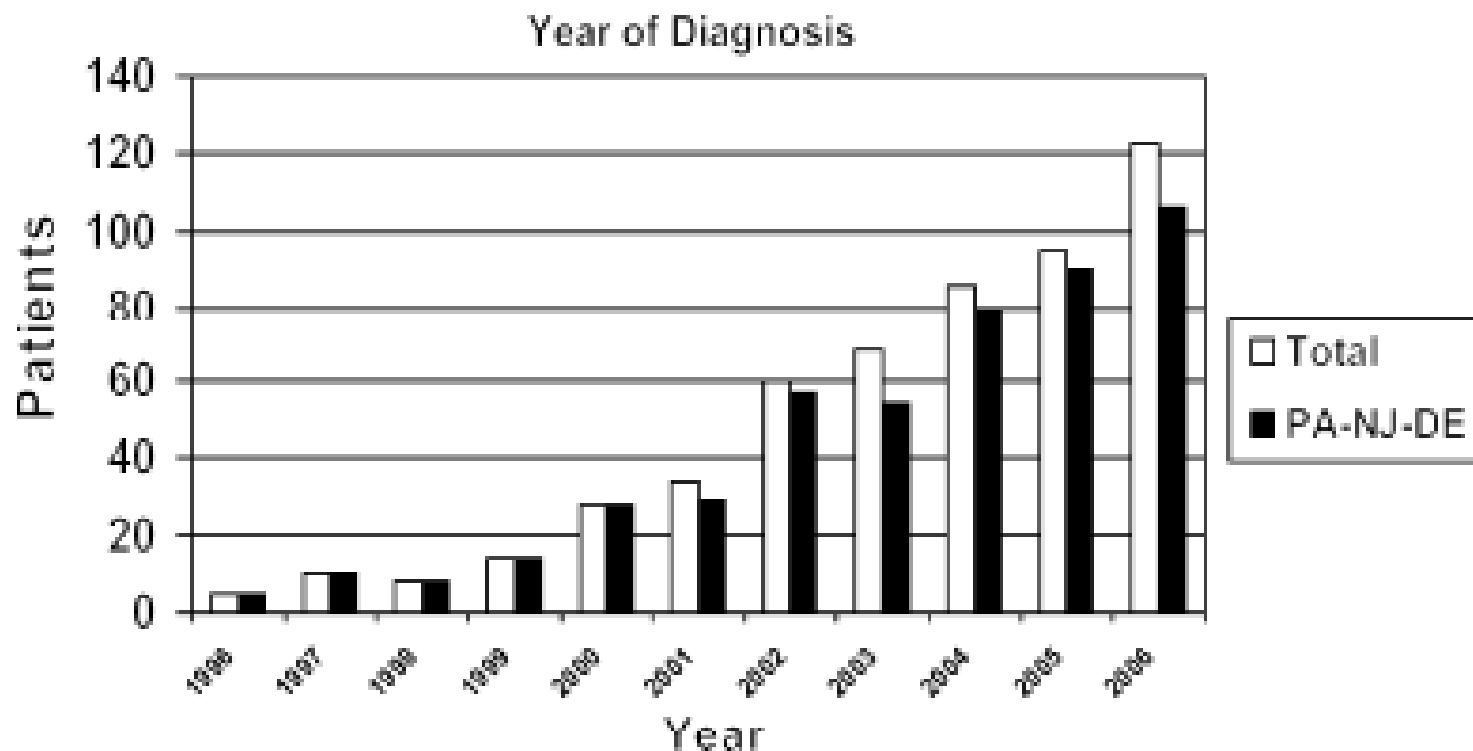
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- 620 patients in database recently reviewed over 14 years
  - 2 new cases in 1994
  - 72 new cases in 2003
  - 124 new cases in 2006.
- Currently, we have approximately 1000+ patients



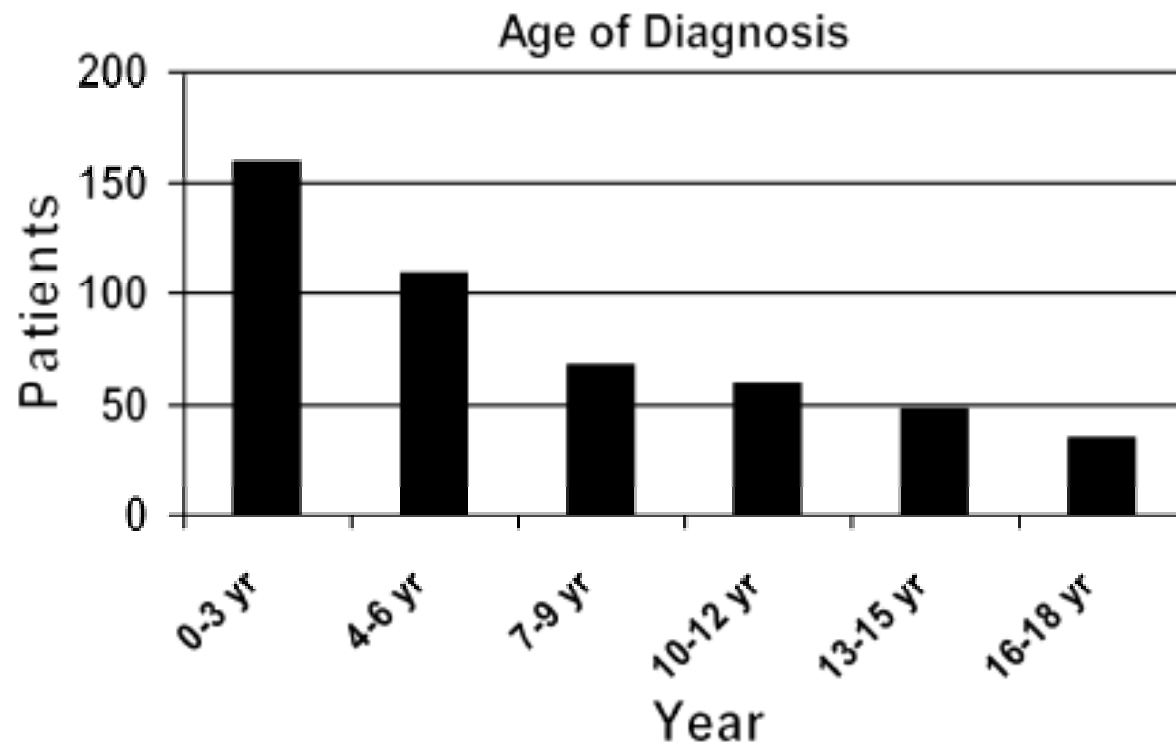
Prevalence thought to be: 1 in 2500

## Numbers of new cases on the rise





## Age at presentation





# Symptoms at presentation

Symptoms at presentation	Median age $\pm$ standard deviation, years	Number of patients
Failure to thrive /feeding difficulties	2.8 $\pm$ 3.2 years	118
Gastroesophageal reflux or vomiting	5.1 $\pm$ 4.1 years	158
Abdominal pain	9.0 $\pm$ 3.0 years	88
Food impaction/dysphagia	11.1 $\pm$ 4.5 years	62

Spergel JM, et al. JPGN 2009;48: 30-36.



## Concomitant atopy

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- 620 pediatric patients, two thirds of patients with EE had concomitant atopy
  - 231 had asthma (37%)
  - 243 had allergic rhinitis (39%)
  - 78 had atopic dermatitis (13%)
  - These numbers are approximately three times higher than what is expected in the general population.



# Prevalence of atopy: in general pediatric population and EE

Author/population	Food Allergy	Asthma	Allergic Rhinitis	Atopic Dermatitis
General Population	3%	8.5%	25%	10%
Spergel et al. <b>620</b> Philadelphia, PA	5.7%	37%	39%	13%
Assa'ad et al <b>89</b> Cincinnati, OH	9%	39%	30%	19%
Sugnanam et al <b>45</b> Australia	24%	66%	93%	55%
Guajardo et al. <b>39</b>	23%	38%	64%	26%

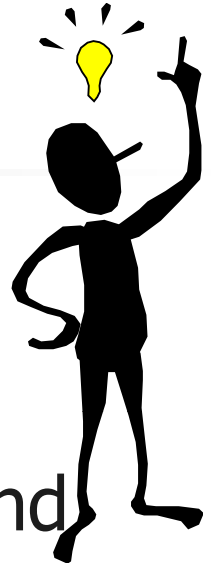
Spergel et al JPGN 2009;48; Assa'ad et al J Allergy Clin Immunol 2007; Sugnanam et al Allergy 2007; Guajardo et al J Pediatr 2002



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## Once the diagnosis is confirmed

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- Allergy referral: relationship between EE and foods
- Historical background
  - Winter et al, 1982
    - “Eosinophils are a diagnostic criterion for GERD”
  - Kelly, Sampson, et al, 1995
    - “Eosinophilic esophagitis attributed to gastroesophageal reflux: improvement with an amino acid-based formula”



## EE and elemental diet

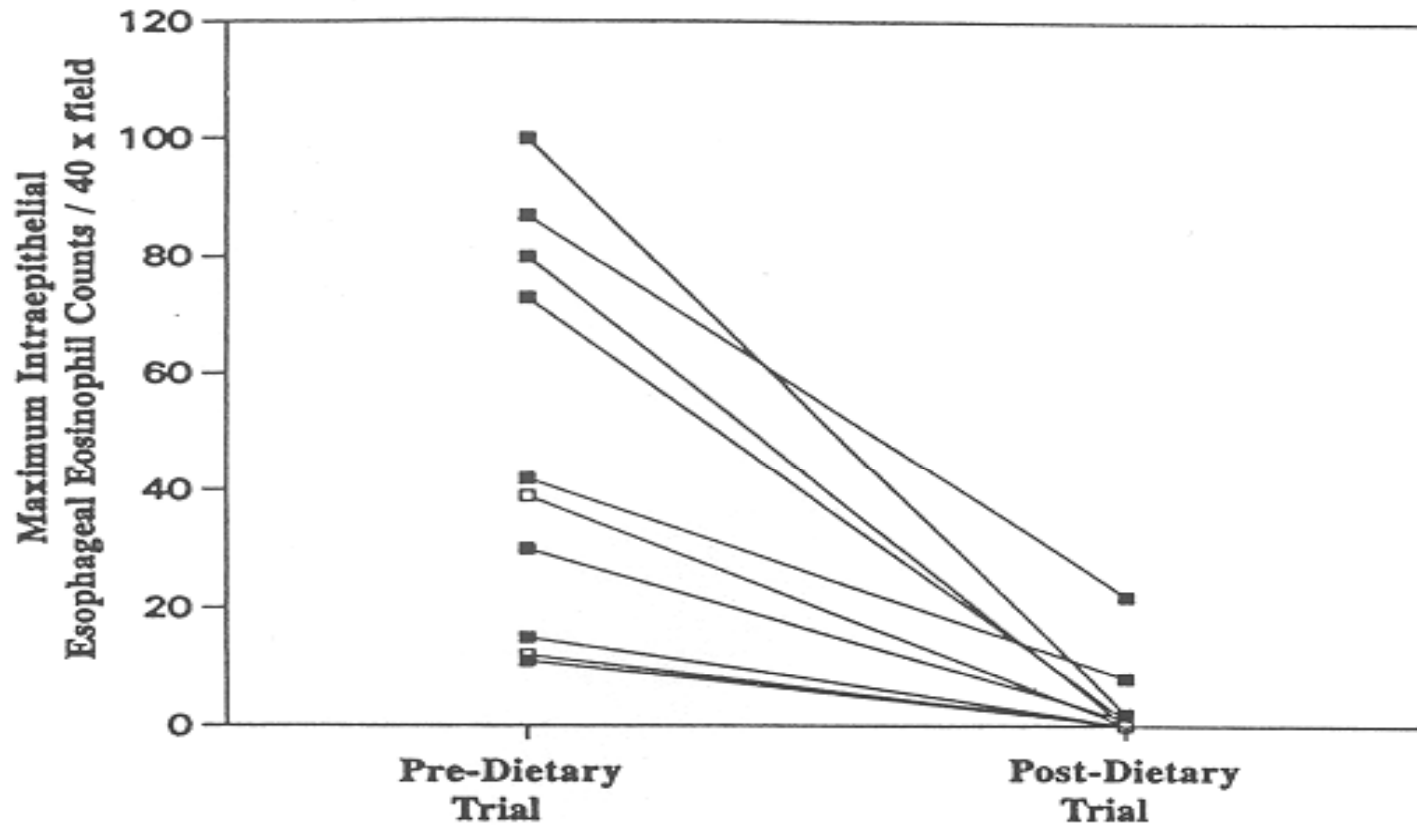
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- 10 children with GERD symptoms
  - Failed treatment for 6 to 78 months with reflux medications
- Workup
  - Negative for other GI disease: Crohn's, Celiac, etc
  - Eosinophil counts were elevated (15 to 100 cells/hpf)
- Patients improved on elimination diet with Neocate<sup>®</sup> or steroids.

# EE and elemental diet

1508 KELLY ET AL.

Kelly KJ,... Sampson HA. Gastroenterology 1995; 109:1503-12





# Eosinophilic Esophagitis:

## Food allergy: IgE and non-IgE mechanism

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- So, if patients improved with an elemental formula, then food must be a cause in many patients with EE
- How do we determine which food?
  - Skin prick testing
  - Patch testing
  - Food elimination of most common foods
  - Guess?



# Food hypersensitivity syndromes

IgE

Non-IgE

Immediate Hypersensitivity  
Oral Allergy Syndrome

Eosinophilic Esophagitis  
Eosinophilic Gastroenteritis

Dietary Protein Enterocolitis  
Dietary Protein Enteropathy  
Dietary Protein Proctitis



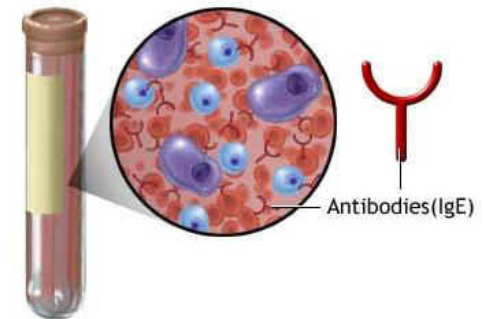
## IgE mediated: skin prick

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- Prick puncture tests
  - Small drop of antigen or fresh food on forearm (occasionally on back) followed by prick and immediate reaction occurs
  - If only prick testing is performed, 50% improvement

# IgE mediated: *in vitro* testing

- Immuno-cap
  - *In vitro* testing for identifying food specific IgE antibodies
  - NOT routinely recommended in patients with EE





## Why patch testing?

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- 61 of 183 patients with eczema had concomitant gastrointestinal reaction
- Delayed vomiting and diarrhea after food challenge (noted in 80% patch test positive compared to 25% with positive skin prick)
  - Isolauri and Turjanmaa, JACI 1996.



# CHOP: EE initial studies

- 26 patients with EE
- Skin test and patch test
- Avoidance
- 75% improved
- Elemental diet helped remaining



- Spergel et al JACI 2002



## Non IgE mediated: Patch testing

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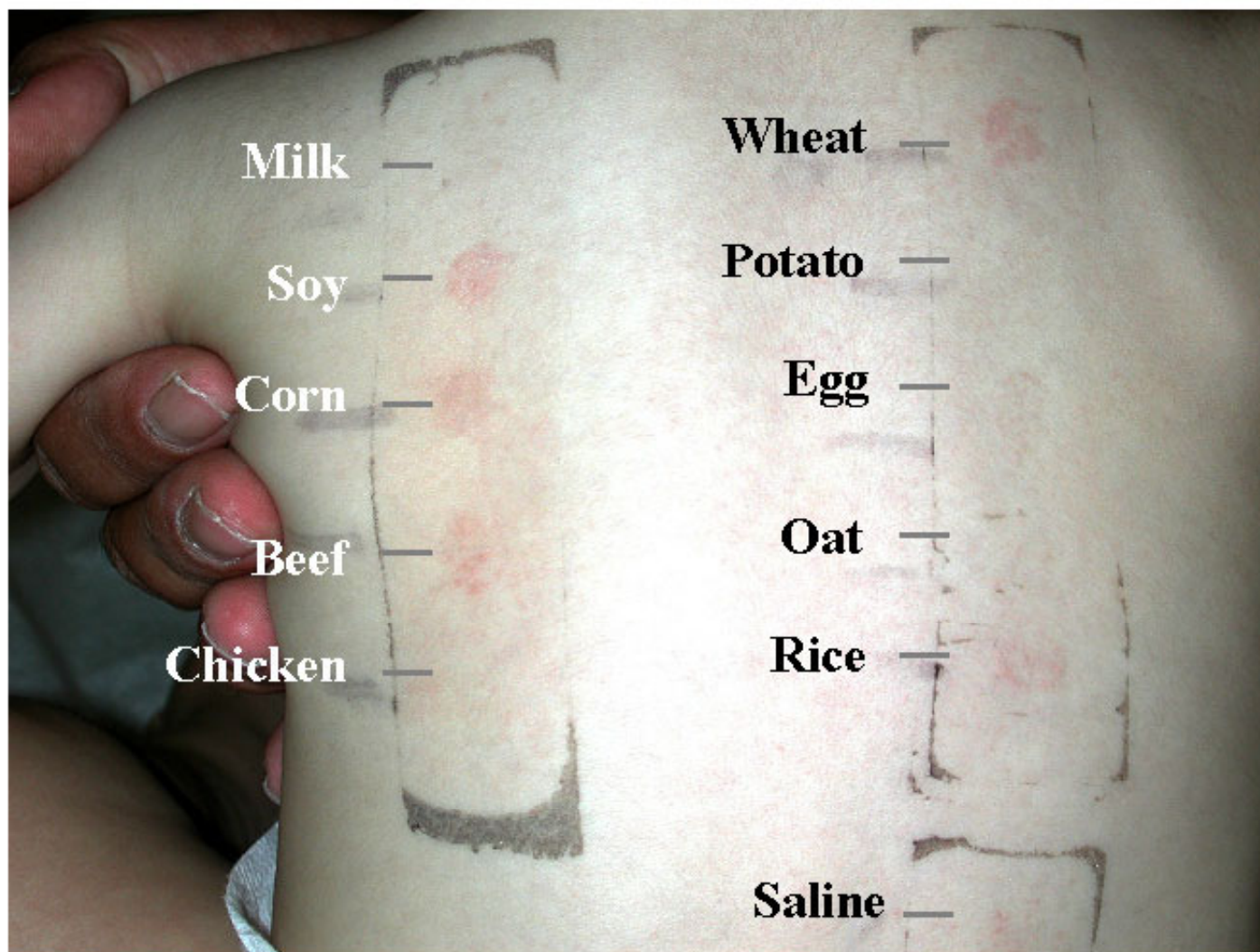
- Prolonged contact of allergen to skin
- Mimic similar non-IgE mediated immune response
- Same concentration of food in patch that is ingested
  - 1 gram of dry food per mL
    - Grains, eggs, soy
  - 3 grams of dry food per mL
    - Milk

# Optimization of testing conditions

- Patients must be off oral steroids or systemic immunosuppressants for a month and off topical steroids or immunosuppressants for a week
- Aluminum finn chambers; Optimal size 12-mm chamber
- Occlusion time: 48 hours; Evaluation time: 72 hours



- No difference in age of patient and predictive capacity



# Side effects of patch testing



- Contact reactions
- Irritation reactions
- Abdominal discomfort?
- Vomiting?
- Scarring?—very, very rare



## CHOP allergy approach to EE

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- All patients have both skin testing and patch testing to foods in child's diet (aeroallergens as needed)
- Other atopic conditions are diagnosed and treated aggressively



## CHOP allergy approach to EE

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- Restricted diet based upon positive results.
- If no identified positive foods:
  - Directly to elemental diet
  - Remove top foods known to cause condition.
- Repeat endoscopy after 8 to 12 weeks of dietary restriction (depending on food) & PPI
  - If normal, one of avoided foods
  - If abnormal, recommend elemental diet



## CHOP most recent testing data

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- Skin prick testing: 109 positive and 45 negative
  - Corn, wheat, soy, milk, beef, rice, chicken, egg, rye, oat, and potato
- Patch testing: 128 positive and 26 negative
  - Milk, egg, soy, peanut, pea, wheat, beef, chicken, corn, and potato
- 8 had negative patch and skin tests





## So...how did we do?

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- No results to date: 12 patients
  - 7 patients were lost to follow-up
- 71% (121 patients) had complete resolution of symptoms and normalization of biopsies
- 15% (10 patients) had partial improvement\*
- 14% (14 patients) reported no improvement\*
  - \* 6/24 pts admitted to cheating on diet



## Predictive values for individual foods...

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- 104 patients with  $> 20$  eos/hpf
  - Removal of a single food leading to normal esophageal biopsy (0 eosinophils/HPF).
    - And/or
  - Addition of a single food leading to increased esophageal eosinophils on biopsy after a previously normal biopsy.



# Allergy testing

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- Combination of two testing methods
  - NPV
    - 88% to 100% for all foods except milk
    - 41% for milk
  - PPV
    - > 74% for the most common foods (milk, egg, and soy)
    - Less as the food became a less common cause
  - Sensitivity
    - 77 to 97% depending on the food



# We are not the only ones...

## dietary restrictions

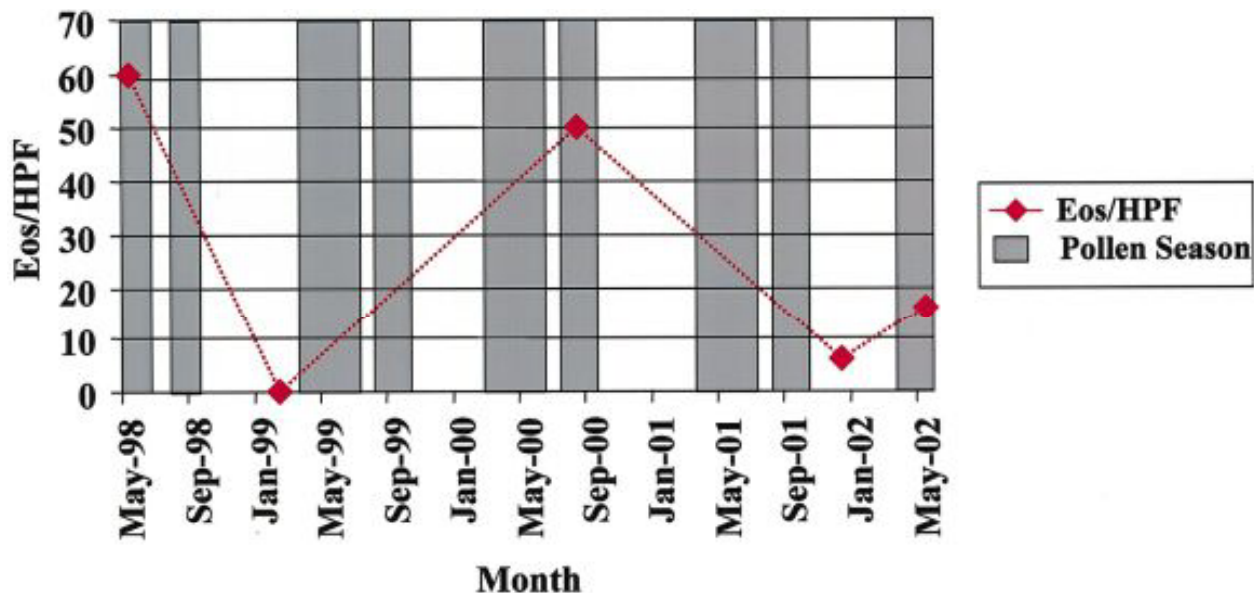
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- 60 total pediatric patients:
  - 25 elemental diet and 35 restricted diet
- Removed milk, egg, soy, wheat, peanuts and seafood
- Both groups improved
  - 88% elemental diet <10 eos/hpf
  - 74% restricted diet <10 eos/hpf

■ Kagalwalla, Clin Gastroenterol Hepatol 2006(4):1097-1102.

# Role of aeroallergens

- One patient where significant role
- Partial role in many others





# Treatment

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- Why treat?
  - Strictures
  - Hiatal hernia
  - No evidence of increased cancer risk
- Therapeutic options
  - Dietary
  - Medications
  - Dilations



# Therapeutic options

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- Dietary
  - Restriction
  - Elimination
- Advantages
  - Cures problem
- Disadvantages
  - Restricted diet
  - Social and behavioral issues



# Therapeutic options

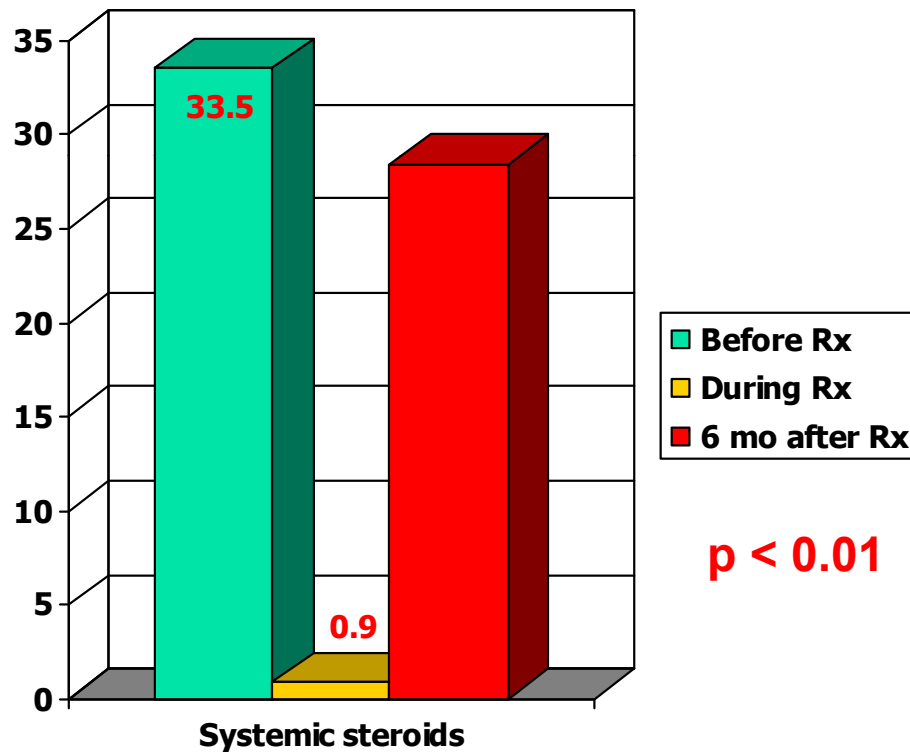
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- Medications

- Gastrochrome (not effective)
- Leukotriene receptor antagonists (? symptom, same histology)
- Systemic steroids
- Topical (“swallowed”) steroids
- Anti-IL5 (in study)



# Therapeutic Options: Systemic Corticosteroids



39 patients

Age:  $8.2 \pm 2.9$  years

Solumedrol 1.5 mg/kg

4-5 weeks

Liacouras, et al. Clin Gastro  
& Hep, 2005.



# Therapeutic options: Systemic Corticosteroids

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- Advantages

- Significantly improves symptoms acutely
- Normalizes esophageal tissue

- Disadvantages

- Cannot be used chronically
- Severe side effects
  - bone, growth, mood, etc.



## Therapeutic options: “Swallowed” inhaled steroids

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- 13 patients treated with fluticasone
  - Max dose (440 mcg BID) for 8 weeks
  - Treated for a longer period of time
- 11 patients – post treatment had EGD
  - All visually still looked abnormal
  - Microscopically, eos improved in all pts
- 2 pts – esophageal candidiasis
  - Teitelbaum et al, Gastroenterology, 2002.



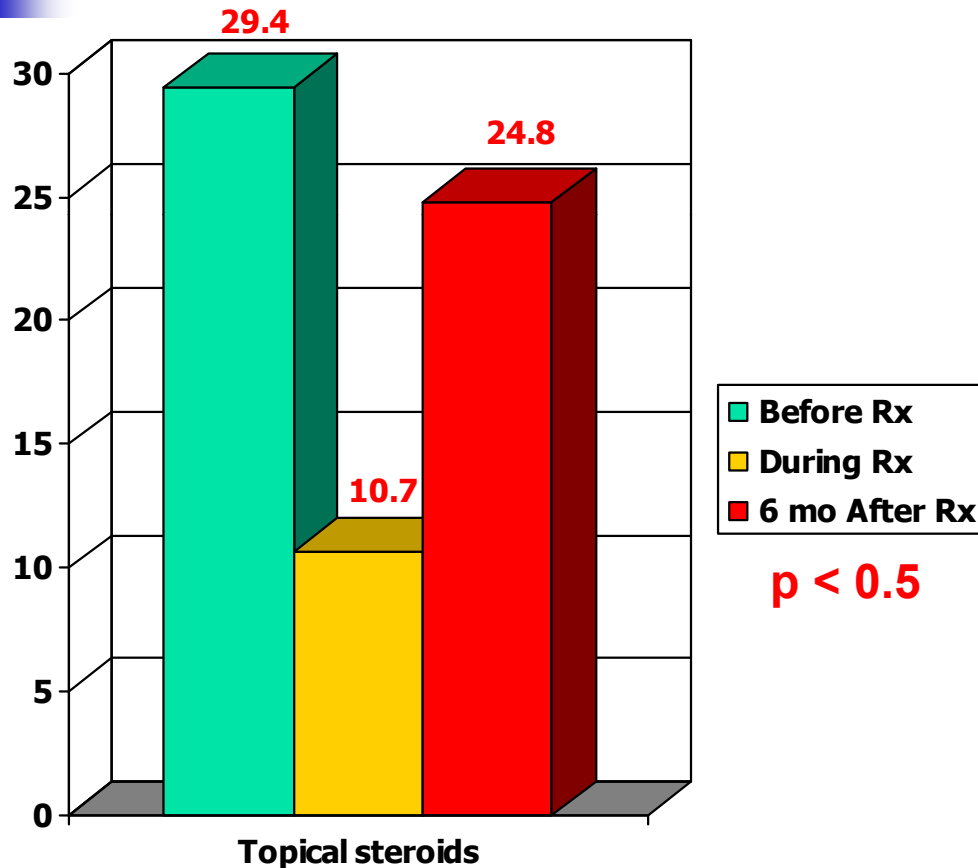
## Therapeutic options: “Swallowed” inhaled steroids

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- 20 pts with EE treated with swallowed fluticasone (avg. daily dose 880 mcg)
- 16/20 pts normalized esophagus (eos)
- 4/20 pts developed esophageal candidiasis
  - Noel, et al; Clin Gastro & Hep, 2004.

# Therapeutic options: “Swallowed” inhaled steroids

# of  
eos



12 patients  
Age:  $8.7 \pm 2.6$   
Fluticasone  
110-220  $\mu\text{g}$  (2) BID  
6-8 weeks

Liacouras, et al. Clin Gastro  
& Hep, 2005.



# Therapeutic options: “Swallowed” inhaled steroids

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- Viscous budesonide: Budesonide 0.5 plus 5 packets of Splenda) swallow (slows transit time)
  - 2 doses (1 mg < 10 years and 2 mg >10 years)
- 20 patients
  - 16 responders (80%)
  - 1 partial
- Side effects
  - Nausea, vomiting
  - Abdominal pain
  - Heartburn



## Therapeutic options: Anti-IL-5

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- Open label phase I/II study: safety and efficacy
  - 4 adult patients with EE
    - Treated weeks 8, 12, 16
    - Biopsy at weeks 8 and 20
  - Esophageal & blood eosinophilia decreased
  - Better clinical outcome and improved quality of life
- Awaiting recent results from larger trial including pediatrics

Stein et al, JACI, 2006.



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# Public awareness

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- APFED

American Partnership for  
Eosinophilic Disorders

[www.apfed.org](http://www.apfed.org)

- Food allergy network

[www.foodallergy.org](http://www.foodallergy.org)



## Other concerns

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- We have had a handful of patients whose endoscopy was once normal on a food and then over time, developed esophageal eosinophils to that food.
- We have also had patients with IgE mediated reactions to milk, outgrow IgE mediated sensitivity, then developed esophageal eosinophils to the food.
- Very few patients have outgrown all foods; thus, thought to be a chronic condition



## References: EE

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EE

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- Brown-Whitehorn TF and CA Liacouras. Eosinophilic Esophagitis. *Current Opinions in Pediatrics* 2007;19:575-580.
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